Cancel claims 2, 11, 20, 29, 30, 33-61 and 73.

REMARKS

The pending claims in the application are 1, 3-10, 12-19, 21-28, 31, 32, 62-72 and 74-76.

Cancellation of Claims 35-61 and Withdrawal of Claims 62-65 with Request for Rejoinder

In the February 14, 2002 Office Action, the Office imposed a four-way restriction requirement against claims 1-65 and required election of one of the following groups:

I. Claims 1-34, drawn to a fusion protein exhibiting a phase transition;

II. Claims 35-61, drawn to DNA encoding protein of Group I, expression vectors, host cells and recombinant production of said protein;

III. Claim 62, drawn to a method of optimizing size of an ELP expression tag; and

IV. Claims 63-65, drawn to a method of purification of fusion peptides.

On March 14, 2002, applicant elected, with traverse, Group I.

Correspondingly, applicant has cancelled claims 35-61 (Group II) herein, and acknowledges the Office's withdrawal of non-elected claims 62 (Group III) and 63-65 (Group IV), with reservation of the right to rejoin the Group III and Group IV claims at a later time in the prosecution of this application, under the provisions of MPEP §821.04, or alternatively, with reservation of the right to file divisional application(s) directed to the subject matter of those claims if rejoinder is not effected.

In accordance with Office guidelines recited in MPEP §821.04, elected composition claims found to recite patentable subject matter may be rejoined with provisionally withdrawn method of use and/or method of making type claims and examined in an originally filed application provided the method of use or method of making claims recite compositions corresponding to those found to be patentable during examination of the elected invention.

Upon the Office's confirmation of patentable subject matter in the composition claims 1, 3-10, 12-19, 21-28, 31, 32, 66-72 and 74-77, the withdrawn method claims 62-65, which are directed to methods for using the compositions recited in claims 1, 3-10, 12-19, 21-28, 31, 32, 66-72 and 74-76, are requested to be taken up for examination and to be rejoined to the allowed elected claims.

Objections to the Drawings

Applicant notes the Draftman's and Examiner's objections to the drawings. **The informalities will be corrected and submitted to the Office under separate cover, within the shortened statutory period ending on February 18, 2003.**

Objections to the Claims

not corrected
tendonmistet vs tendons2et

In the November 18, 2002 Office Action, claims 71-75 were objected to because abbreviations were used in claims for the first time. Accordingly, claim 71 was amended to include "elastin-like peptide" in place of the acronym ELP, thereby obviating this objection.

Applicant notes the Examiner's statement that should claim 27 be found allowable, claim 29 will be objected to under 37 C.F.R. §1.75 as being a substantial duplicate thereof. It is noted that claim 29 has been cancelled herein by applicant.

Rejection of Claims and Traversal Thereof

In the November 18, 2002 Office Action:

claims 1-8, 20, 25, 26, 31 and 33 were rejected under 35 U.S.C. §112, second paragraph;

claims 1-11, 22-24, 26, 29 and 33 were rejected under 35 U.S.C. §112, first paragraph as containing subject matter which was not described in the specification;

claims 1-34 and 66-75 were rejected under 35 U.S.C. §112, first paragraph for lack of enablement; and

claim 71 was rejected under 35 U.S.C. §102 (b) as being anticipated by McPherson et al. (D.T. McPherson, C. Morrow, D.S. Minehan, J. Xu, E. Hunter, D.W. Urry, "Production and Purification of a

Recombinant Elastomeric Polypeptide G-(VPGVG)$_{19}$-VPGV, from *Escherichia coli*," *Biotechnol. Prog.*, 8, 347-352 (1992)).

These various rejections are traversed and reconsideration of the patentability of the claims, as amended, is requested in light of the following remarks.

Rejection under 35 U.S.C. §112, second paragraph

In the November 18, 2002 Office Action, claims 1-8, 20, 25, 26, 31 and 33 were rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Office made numerous rejections and applicant addresses each in turn below.

(1) Claims 1-7, 25 and 26 were rejected under §112, 2nd paragraph, based on the recitation of the terms "biological molecules" and "biologically active molecule" in claim 1. According to the Office, a broad range and a narrow range that falls within the broad range are recited in the same claim, rendering the claim indefinite. Accordingly, claim 1 was amended to recite only "biological molecules," wherein the biological molecules were further defined to include peptides and proteins (for Markush group support, see specification on page 9, lines 7-9). ok

(2) Claim 1 was further rejected for reciting the phrase "a phase transition joined to the biologically active molecule," which the Office states improperly joins a phenomenon (the phase transition) to a molecule. Claim 1 was amended to overcome this rejection by clearly defining that the phase transition protein, which can exhibit an inverse phase transition, is joined to the biological molecule of 1(a). ok

(3) Claim 2 was further rejected for reciting the term "non-peptide proteins." This rejection is moot in view of the cancellation of claim 2. ok

(4) Claim 8 was rejected for reciting the phrase "the protein of interest," thus rendering the claim indefinite. Claim 8 was amended to recite "the biological molecule of interest." ? spread number correct

(5) Claim 20 was rejected because, according to the Office, it does not further limit the base claim (claim 1). This rejection has been rendered moot by the cancellation herein of claim 20. ok

(6) Claim 25 was rejected for failing to indicate what applicant meant when claiming that any of the biological molecules (a), (b) and (c) may be produced recombinantly. Accordingly, applicant has amended claim 25 to include only the recombinantly formed fusion protein.

(7) Claim 26 was rejected for failing to indicate what applicant meant by the phrase "synthetically produced." Claim 26 has been amended to include fusion proteins of claim 1 comprising recombinantly produced parts 1(a), 1(b) or 1(c).

(8) Claims 31 and 33 were rejected because part (c) of each was directed to itself. Applicant has cancelled claim 33 and amended claim 31 to overcome this rejection.

In light of the foregoing, applicant respectfully requests that the rejection of claims 1, 3-8, 25, 26 and 31, on the basis of indefiniteness, be withdrawn.

Rejection under 35 U.S.C. §112, first paragraph

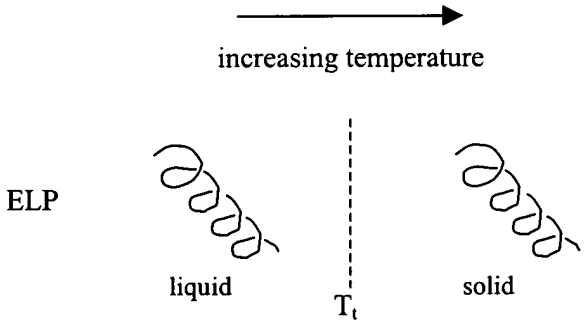
In the November 18, 2002 Office Action, claims 1-11, 22-24, 26, 29 and 33 were rejected under 35 U.S.C. §112, first paragraph for containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Applicant traverses this rejection and requests reconsideration of claims 1, 3-10, 22-24, and 26, as amended, in light of the following remarks.

(1) Claims 1-11 were rejected under 35 U.S.C. §112, 1st paragraph, on the basis of written description. According to the Office, neither the claims nor the specification set forth (1) the structures of the fusion protein (see Nov. 18, 2002 Office Action, page 6, lines 22-23) or (2) "which features of the biologically active proteins ensure the capacity of exhibiting the phase transition of the fused protein" (see Nov. 18, 2002 Office Action, page 7, lines 1-2). Applicant vigorously disagrees.

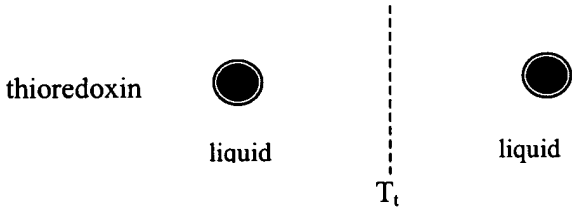
Applicant's invention relates to a fusion protein that exhibits a phase transition, wherein the fusion protein comprises (a) a biological molecule of interest, such as a peptide or a protein, (b) an elastin-like peptide (ELP) tag which undergoes an inverse phase transition and (c) optionally a spacer. The ELP tag can be attached to any peptide or protein of interest to form the ELP-tagged fusion protein of the present invention wherein the ELP-tagged fusion protein exhibits an inverse phase transition.

By tagging the ELP to the biological molecule of interest, the ELP-tagged fusion protein retains the functionality of the biological molecule, while at the same time retaining the inverse transition behavior of the ELP tag. This duality of function facilitates separation and purification of the fusion protein from a solution using the inverse transition cycling (ITC) technique, wherein the ELP-tagged fusion protein is insoluble in aqueous solutions at temperatures greater than a transition temperature (T_t) and can be readily separated from the supernatant solution. For example, the inverse transition behavior of ELP-tagged thioredoxin relative to ELP and thioredoxin alone, is illustrated in Figure 1 below.

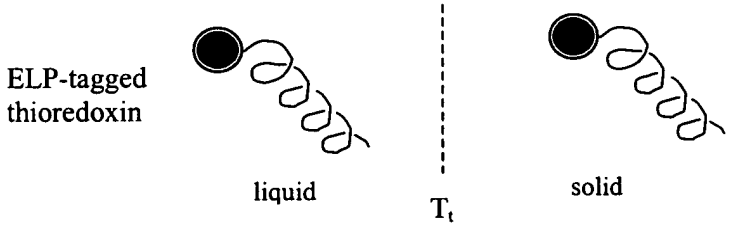
Figure 1:



a. As shown above, at temperatures greater than the T_t, an ELP molecule undergoes an inverse transition from liquid to solid.



b. However, as shown above, the protein thioredoxin does not undergo an inverse transition from liquid to solid, regardless of the T_t.



c. Upon attachment of the ELP-tag to the thioredoxin to form an ELP-thioredoxin fusion protein, the fusion protein will undergo an inverse transition from liquid to solid at temperatures greater than T_t.

Applicant submits that the structure of the fusion protein has been adequately set forth in the specification and claims (see for example Figs. 11 and 12). Further, applicant points out that it is not the biologically active proteins alone that exhibit the phase transition, as suggested by the Office, but rather the ELP-tagged fusion protein (see also illustration above). Applicant has adequately set forth in the specification and claims that ELP-tagged fusion proteins exhibit a phase transition (see for example Fig. 4).

Moreover, applicant has shown that separation and purification can be effectuated using biological molecules having extremely different expression and physico-chemical properties. Thioredoxin is comprised of 108 amino acids and is a soluble, over-expressed protein. In contrast, tendamistat is comprised of 74 amino acids and is poorly expressed as an insoluble protein. In the case of tendamistat, only after tagging the protein to the ELP is the ELP-tagged fusion protein soluble in aqueous solution below the appropriate T_t. Thereafter, the ITC technique can be used to effectively separate the ELP-tendamistat fusion protein from the supernatant solution. Knowing that any peptide or protein can be tagged with ELP, applicant has demonstrated that regardless of the physico-chemical properties of the expressed peptide or protein, the inverse transition behavior of the ELP tag is retained in the ELP-tagged fusion protein.

In short, applicant manifestly was in possession of the claimed invention at the time the application was filed. Accordingly, applicant respectfully requests that the rejection of claims 1 and 3-10, as amended, on the basis of written description be withdrawn.

(2) Claims 2-3 and 5-7 were rejected because the claims were directed to a large and variable genera that are not described by structure and function by applicant. Applicant has cancelled claim 2; claims 3 and 5-7 are supported by the disclosure.

Claim 3 relates to a fusion protein wherein the biological molecule comprises a peptide. According to the definition on page 9, lines 8-9, "peptide" is defined as shorter polypeptides having less than 100 amino acid residues. As introduced hereinabove, tendamistat is comprised of 74 amino acids therefore making it a "peptide" for purposes of applicant's invention. Applicant has thoroughly shown that an ELP-tagged fusion protein comprising tendamistat exhibits a phase transition. Accordingly, claim 3 is supported by the specification.

Claims 5-7 relate to a fusion protein wherein the biological molecule comprises a therapeutic protein, an enzyme useful in industrial biocatalysis and an antibody or antibody fragment, respectively. Because enzymes and antibodies are proteins, one of ordinary skill in the art will be able to attach an ELP-tag to the proteins of claims 5-7 to form an ELP-tagged fusion protein of the invention. Applicant has demonstrated that regardless of the solubility of the protein in aqueous solution, once an ELP tag is attached to the protein, the ELP-tagged fusion protein has the ability to undergo a phase transition. The Office is reminded that the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. See MPEP §2163(II)(3)(a)(ii). Accordingly, applicant submits that claims 5-7 are supported by the specification.

(3) Claims 11, 29 and 33 were rejected because the specification does not teach the structure of all possible proteins exhibiting a β-turn . Applicant has cancelled claims 11, 29 and 33. Replacing claim 11, claim 76 has been added to read on claim 12 wherein the phase transition protein comprising oligomeric repeats of the pentapeptide VPGXG exhibits a β-turn.

(4) Claims 22-24 were rejected because the specification is silent about the structure of a fusion protein containing any signal peptide. Applicant vigorously disagrees.

The Office bears the initial burden of presenting a *prima facie* case of unpatentability. *In re Oetiker*, 24 U.S.P.Q.2d 1443 (Fed. Cir. 1992). In order to meet the burden of proof with regards to the written description requirement, the Office must provide reasons why one of ordinary skill in the art would not consider the description sufficient. *In re Alton*, 37 U.S.P.Q.2d 1578 (Fed. Cir. 1996). Applicant contends that the Office has not satisfied this burden.

The Office's attention is directed to the specification, pg 6, lines 20-23, wherein applicant teaches that:

> "The [fusion proteins] FPs of the invention may also comprise a signal peptide, which is preferably cleavable from the fusion protein by enzymatic cleavage. The signal peptide preferably directs secretion of the fusion protein from the cell, so that the FP may readily be isolated from the medium of an active culture of recombinant cells genetically modified to produce the FP."

See also page 7, lines 22-24 and page 18, lines 16-18.

The Office is reminded that information which is well known in the art need not be described in detail in the specification. *See e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80 (Fed. Cir. 1986). Because the use of signal peptides to specify the destination of nascent proteins is well known in the art, the description provided satisfies the requirement that the inventor had possession of the subject matter of the invention as of the filing date thereof.

As such, applicant respectfully requests that the rejection of claims 22-24 on the basis of written description be withdrawn.

(5) Claim 26 was rejected because applicant did not describe any protein consisting of parts 1(a), 1(b) and 1(c) that were produced synthetically. Claim 26 has been amended to include fusion proteins of claim 1 comprising recombinantly produced parts 1(a), 1(b) or 1(c), thereby obviating this rejection.

In conclusion, applicant submits that claims 1, 3-10, 22-24, and 26, as amended, are adequately described in the specification and are therefore patentable. Hereinafter, the Office is reminded that it has the burden of "presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined in the claims." *In re Wetheim*, 191 U.S.P.Q. 90 (CCPA 1976). Applicant submits that one of ordinary skill in the art reading the instant specification would be compelled by such disclosure to the conclusion that applicant fully possessed the invention at the time the application was filed. Withdrawal of the §112, first paragraph rejections is therefore requested.

In the November 18, 2002 Office Action, claims 1-34 and 66-75 were rejected under 35 U.S.C. §112, first paragraph because the specification does not enable any person skilled in the art to which it pertains to make and use the invention commensurate in scope with these claims. Applicant traverses this rejection and requests reconsideration of claims 1, 3-10, 12-19, 21-28, 31, 32, 66-72 and 74-75, as amended, in light of the following remarks.

The Office acknowledges that the knowledge of the production of fusion proteins "is well developed and [the] skills of artisans [are] highly developed" (see Nov. 18, 2002 Office Action, page 11, lines 9-10), yet the Office contends that not only does one have to make a fusion protein (which the Office admits is a highly developed skill), but more important, "the fusion protein has to exhibit the phase transition phenomenon" (see Nov. 18, 2002 Office Action, page 11, lines 12-13). According to the

Office, the experimentation necessary to check for the capacity of phase transition is out of the realm of routine experimentation.

Claim 1, as amended, recites *inter alia*:

> **"A fusion protein exhibiting a phase transition, the fusion protein comprising:**
> **(a) one or more biological molecules selected from the group consisting of peptides and proteins;"**

As such, applicant has limited the scope of the claimed invention to fusion proteins comprising the molecules of the Markush group in (a), the ELP-tag (b) and optionally a spacer (c).

As stated hereinabove, the disclosure enables one skilled in the art to make and use ELP-tagged fusion proteins that exhibit a phase transition, regardless of the physico-chemical properties of the biological molecule of interest (see thioredoxin (protein) and tendamistat (peptide)). In both cases, regardless of the extent of expression and the solubility of the biological molecule of interest, the ELP-tagged fusion protein was successfully separated from the other components in the milieu.

With regard to the Office's assertion that the "experimentation left to those skilled in the art is improperly extensive and undue" (see Nov. 18, 2002 Office Action, page 12, lines 7-8), the Office is reminded that even where some experimentation is necessary to reduce the invention to practice, the enablement requirement is satisfied where: (1) the experimentation is routine; or (2) the specification provides "a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. *See PPG Indus. Inc. v. Guardian Indus. Corp.*, 27 U.S.P.Q.2d 1618, 1623 (Fed. Cir. 1996). Clearly, determining whether an ELP-tagged fusion protein undergoes a phase transition is well within the skill of those in the field of applicant's claimed invention. As such, applicant's disclosure thoroughly enables one skilled in the art to obtain, without undue experimentation, the claimed compositions of the present invention. Applicant requests that the rejection of claims 1, 3-10, 12-19, 21-28, 31, 32, 66-72 and 74-75, as amended, on the basis of enablement be withdrawn.

Rejection under 35 U.S.C. §102(b)

In the November 18, 2002 Office Action, claim 71 was rejected under 35 U.S.C. §102(b) as being anticipated by McPherson et al.[2]. Applicant respectfully traverses this rejection and submits that applicant's claimed invention, as amended, is not anticipated by McPherson et al.

Claim 71, as amended, recites:

> **An elastin-like peptide fusion protein in a composition comprising a solvent medium in which the ELP fusion protein exhibits an inverse phase transition upon a predetermined change of composition condition.**

Applicant submits that McPherson et al. does not disclose a ELP fusion protein which exhibits an inverse phase transition. Thus, it is clear that McPherson et al. does not anticipate claim 71, as amended herein. Accordingly, reconsideration and withdrawal of the rejection is requested.

Fees Payable

Applicant has added one (1) additional dependent composition claims, however, since claims 2, 11, 20, 29, 30, 33-61 and 73 have been cancelled herein, there is no net addition of claims beyond the number for which payment previously has been submitted, and therefore no additional fee is due.

If nonetheless it is determined that any fee or charge is properly payable for the entry of this Amendment hereby, the Office is authorized to charge same to Deposit Account No. 08-3284 of Intellectual Property/Technology Law.

CONCLUSION

Based on the amendments made herein and the foregoing remarks, applicant's pending claims 1, 3-10, 12-19, 21-28, 31, 32, 62-72 and 74-76 are in form and condition for allowance. The Examiner therefore is requested to reconsider such claims, and to issue a Notice of Allowance for the present application.

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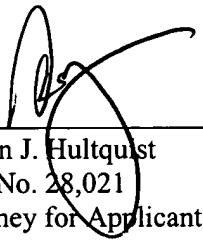
[2] D.T. McPherson, C. Morrow, D.S. Minehan, J. Xu, E. Hunter, D.W. Urry, "Production and Purification of a Recombinant Elastomeric Polypeptide G-(VPGVG)$_{19}$-VPGV, from *Escherichia coli*," *Biotechnol. Prog.*, 8, 347-352 (1992)

Respectfully submitted,



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APPENDIX A

Marked Up Version of Amended Claims

1. (Amended) A fusion protein exhibiting a phase transition, the fusion protein comprising:

(a) one or more biological molecules selected from the group consisting of peptides and proteins;

(b) one or more phase transition proteins that exhibit[ing] an inverse phase transition, wherein the one or more phase transition proteins are joined to the [biologically active] biological molecule(s) of (a); and

(c) optionally, a spacer sequence separating any of the phase transition protein(s) of (b) from any of the biological molecule(s) of (a).

8. (Amended) The fusion protein of claim 7 wherein the antibody or antibody fragment has affinity for a [protein] biological molecule of interest, and wherein upon binding to the [protein] biological molecule of interest, the fusion protein retains some or all of its phase transition character.

12. The fusion protein of claim 1 wherein the one or more phase transition protein(s) of 1(b) comprises oligomeric repeats of the pentapeptide Val-Pro-Gly-X-Gly, wherein X is any natural or non-natural amino acid residue, and wherein X optionally varies among oligomeric repeats.

21. (Amended) The fusion protein of claim [20] 1 wherein the spacer sequence comprises a proteolytic cleavage site.

25. (Amended) The fusion protein of claim 1 wherein the fusion protein [or any of the biological molecule(s) of 1(a), protein(s) of 1(b), and spacer sequence of 1(c) (when present)] is recombinantly produced.

26. (Amended) The fusion protein of claim 1 wherein [the fusion protein or] any of the biological molecule(s) of 1(a), phase transition protein(s) of 1(b), [and] or spacer sequence of 1(c) (when present) is [synthetically] recombinantly produced.

27. (Amended) A fusion protein exhibiting a phase transition, the fusion protein comprising:

(d) one or more protein(s) of interest;

(e) one or more phase transition protein(s) [exhibiting a phase transition] joined at a C- and/or N-terminus of a protein of (a); and

(f) optionally, a spacer sequence separating [the] any of the protein(s) of (a) and[/or] the phase transition protein(s) of (b).

31. (Amended) A fusion protein exhibiting a phase transition, the fusion protein comprising:

(a) a protein of interest;

(b) a phase transition protein joined at a C- and/or N-terminus of the protein of interest; and

(c) optionally, a spacer sequence separating the protein of (a) from the phase transition protein of [(c)] (b).

71. (Amended) An [ELP] elastin-like peptide fusion protein in a composition comprising a solvent medium in which the ELP fusion protein exhibits an inverse phase transition upon a predetermined change of composition condition.

74. (Amended) The ELP fusion protein of claim [73] 71, wherein said composition further comprises a cleavage agent effective to cleave the cleavage site of the ELP fusion protein to yield the protein of interest and the ELP as cleavage products.

76. (Added) The fusion protein of claim 12 wherein the phase transition protein(s) comprise a β-turn structure.

77. (Added) The polynucleotide of claim 35 wherein the phase transition protein(s) of 35(b) comprise a β-turn structure.

APPENDIX B

Clean Copy of All Pending Claims

1. A fusion protein exhibiting a phase transition, the fusion protein comprising:

(a) one or more biological molecules selected from the group consisting of peptides and proteins;

(b) one or more phase transition proteins that exhibit an inverse phase transition, wherein the one or more phase transition proteins are joined to the biological molecule(s) of (a); and

(c) optionally, a spacer sequence separating any of the phase transition protein(s) of (b) from any of the biological molecule(s) of (a).

2. (Cancelled)

3. The fusion protein of claim 1 wherein the biological molecule of 1(a) comprises a peptide.

4. The fusion protein of claim 1 wherein the biological molecule of 1(a) comprises a biologically active protein.

5. The fusion protein of claim 1 wherein the biological molecule of 1(a) comprises a therapeutic protein.

6. The fusion protein of claim 1 wherein the biological molecule of 1(a) comprises an enzyme useful in industrial biocatalysis.

7. The fusion protein of claim 1 wherein the biological molecule of 1(a) comprises an antibody or antibody fragment.

8. The fusion protein of claim 7wherein the antibody or antibody fragment has affinity for a biological molecule of interest, and wherein upon binding to the biological molecule of interest, the fusion protein retains some or all of its phase transition character.

9. The fusion protein of claim 1 wherein the phase transition is mediated by one or more means selected from the group comprising:

(a) changing temperature;

(b) changing pH;

(c) addition of solutes and/or solvents,

(d) side-chain ionization or chemical modification; and

(e) changing pressure.

10. The fusion protein of claim 1 wherein the phase transition is mediated by means comprising raising temperature.

11. (Cancelled)

12. The fusion protein of claim 1 wherein the one or more phase transition protein(s) of 1(b) comprises oligomeric repeats of the pentapeptide Val-Pro-Gly-X-Gly, wherein X is any natural or non-natural amino acid residue, and wherein X optionally varies among oligomeric repeats.

13. The fusion protein of claim 12 wherein the X component(s) of the oligomeric repeats comprise(s) a naturally-occurring amino acid residue.

14. The fusion protein of claim 12 wherein the X component(s) of the oligomeric repeats comprise(s) a non-naturally-occurring amino acid residue.

15. The fusion protein of claim 12 wherein the X component(s) of the oligomeric repeats comprise(s) one or more amino acid residues selected from the group consisting of: alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine and valine residues.

16. The fusion protein of claim 12 wherein any two or more of the oligomeric repeats are separated by one or more amino acid residues which do not eliminate the phase transition characteristic of the fusion protein.

17. The fusion protein of claim 12 wherein the ratio of Val-Pro-Gly-X-Gly oligomeric repeats to other amino acid residues of the ELP is greater than about 75%.

18. The fusion protein of claim 12 wherein the ratio of Val-Pro-Gly-X-Gly oligomeric repeats to other amino acid residues of the ELP is greater than about 85%.

19. The fusion protein of claim 12 wherein the ratio of Val-Pro-Gly-X-Gly oligomeric repeats to other amino acid residues of the ELP is greater than about 95%.

20. (Cancelled)

21. The fusion protein of claim 1 wherein the spacer sequence comprises a proteolytic cleavage site.

22. The fusion protein of claim 1 wherein the fusion protein further comprises a signal peptide.

23. The fusion protein of claim 22 wherein the signal peptide is cleavable from the fusion protein by enzymatic cleavage.

24. The fusion protein of claim 22 wherein the signal peptide directs secretion of the fusion protein from the cell.

25. The fusion protein of claim 1 wherein the fusion protein is recombinantly produced.

26. The fusion protein of claim 1 wherein any of the biological molecule(s) of 1(a), phase transition protein(s) of 1(b), or spacer sequence of 1(c) (when present) is recombinantly produced.

27. A fusion protein exhibiting a phase transition, the fusion protein comprising:

(a) one or more protein(s) of interest;

(b) one or more phase transition protein(s) joined at a C- and/or N-terminus of a protein of (a); and

(c) optionally, a spacer sequence separating any of the protein(s) of (a) and the phase transition protein(s) of (b).

28. The fusion protein of claim 27 wherein the phase transition is mediated by means comprising raising temperature.

29. (Cancelled)

30. (Cancelled)

31. A fusion protein exhibiting a phase transition, the fusion protein comprising:

(a) a protein of interest;

(b) a phase transition protein joined at a C- and/or N-terminus of the protein of interest; and

(c) optionally, a spacer sequence separating the protein of (a) from the phase transition protein of (b).

32. The fusion protein of claim 31 wherein the phase transition is mediated by raising temperature.

33. (Cancelled)

34. (Cancelled)

35. (Cancelled)

36. (Cancelled)

37. (Cancelled)

38. (Cancelled)

39. (Cancelled)

40. (Cancelled)

41. (Cancelled)

42. (Cancelled)

43. (Cancelled)

44. (Cancelled)

45. (Cancelled)

46. (Cancelled)

47. (Cancelled)

48. (Cancelled)

49. (Cancelled)

50. (Cancelled)

51. (Cancelled)

52. (Cancelled)

53. (Cancelled)

54. (Cancelled)

55. (Cancelled)

56. (Cancelled)

57. (Cancelled)

58. (Cancelled)

59. (Cancelled)

60. (Cancelled)

61. (Cancelled)

62. A method of optimizing size of an ELP expression tag incorporated in a polynucleotide comprising a nucleotide sequence encoding a fusion protein exhibiting a phase transition, wherein the fusion protein comprises a protein of interest, said method comprising the steps of (i) forming a multiplicity of polynucleotides comprising a nucleotide sequence encoding a fusion protein exhibiting a phase transition, wherein each of said multiplicity

of polynucleotides includes a different-sized ELP expression tag, (ii) expressing corresponding fusion proteins from said multiplicity of polynucleotides, (iii) determining a yield of the desired protein for each of said corresponding fusion proteins, (iv) determining size of particulates for each of said corresponding fusion proteins in solution as temperature is raised above T_t, and (v) selecting an optimized size ELP expression tag according to predetermined selection criteria for maximum recoverable protein of interest from among said multiplicity of polynucleotides.

63. A method of purification of fusion proteins to yield a protein of interest, comprising forming a polynucleotide comprising a nucleotide sequence encoding a fusion protein exhibiting a phase transition, expressing the fusion protein in culture, and subjecting a fusion protein-containing material from said culture to processing involving centrifugation and inverse transition cycling to recover said protein of interest.

64. The method of claim 63, comprising expressing the fusion protein in culture in a well of a microplate.

65. The method of claim 63, comprising processing the fusion protein-containing material from said culture in a well of a microplate.

66. The fusion protein of claim 9, wherein the phase transition is mediated by addition of solute.

67. The fusion protein of claim 66, wherein the solute comprises an organic solute.

68. The fusion protein of claim 66, wherein the solute comprises an ionic solute.

69. The fusion protein of claim 68, wherein the ionic solute comprises a salt.

70. The fusion protein of claim 66, wherein the salt comprises NaCl.

71. An elastin-like peptide fusion protein in a composition comprising a solvent medium in which the ELP fusion protein exhibits an inverse phase transition upon a predetermined change of composition condition.

72. The ELP fusion protein of claim 71, comprising a protein of interest cleavable from the ELP at a cleavage site of the ELP fusion protein to yield the protein of interest and the ELP as cleavage products.

73. (Cancelled)

74. The ELP fusion protein of claim 71, wherein said composition further comprises a cleavage agent effective to cleave the cleavage site of the ELP fusion protein to yield the protein of interest and the ELP as cleavage products.

75. The ELP fusion protein of claim 74, wherein said cleavage agent is a proteolytic agent effective to proteolytically cleave the cleavage site of the ELP fusion protein.

76. The fusion protein of claim 12 wherein the phase transition protein(s) comprise a β-turn structure.

77. The polynucleotide of claim 35 wherein the phase transition protein(s) of 35(b) comprise a β-turn structure.